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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/690,169	10/21/2003	R. Kent Hermsmeyer	HME/7961.0013	3934

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EXAMINER	
RAMACHANDRAN, UMAMAHESWARI	
ART UNIT	**PAPER NUMBER**
1617	

MAIL DATE	DELIVERY MODE
01/11/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/690,169	HERMSMEYER, R. KENT	
	Examiner	Art Unit	
	Umamaheswari Ramachandran	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/18/2007 has been entered.

Claim 1 has been amended and claims 17-23 are withdrawn from consideration. Claims 1-6 are currently pending and are being examined on the merits herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The amended claim 1, line 3-5 states " "selective estrogen beta receptor agonist that has a higher relative potency for estrogen receptor beta compared to estrogen receptor alpha than that of genistein". The limitation is indefinite because it is not clear from the claim that selective estrogen receptor beta agonist has higher relative potency than genistein or estrogen receptor beta agonist has a higher relative potency for estrogen receptor beta compared to estrogen receptor alpha than genistein's relative potency for estrogen receptor beta compared to estrogen receptor alpha.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 1 is directed to a method for reducing the incidence or severity of vascular hyperreactivity in a patient in need thereof comprising administering to the patient an effective amount of a selective estrogen beta receptor agonist that has a higher relative potency for estrogen receptor beta compared to estrogen receptor alpha than that of genistein. The applicant has pointed to page 5, last 5 lines, figure 3, and in example 8 of the specification for support of the amendment "higher relative potency for estrogen receptor beta compared to estrogen receptor alpha". Pages 5, last 5 lines in the specification teach the compounds (derivative forms of 3βAdiol) pertain particularly to estrogen receptor beta agonists that are selective over estrogen receptor alpha. Example 8 and Figure 3 teaches the estrogen beta receptor activity of several compounds including tamoxifen, 17-β estradiol, estriol, 3βAdiol and epiestriol. Example 8 indicates that epiestriol and 3βAdiol are selective for estrogen beta over estrogen alpha receptors and have beta receptor activity similar to that of estriol and estradiol. The specification provides support that the compounds epiestriol

and 3βAdiol have selectivity towards estrogen beta receptor compared to estrogen alpha receptor. The specification does not provide support to the limitation that estrogen beta receptor agonist that has a higher relative potency for estrogen receptor beta compared to estrogen receptor alpha than that of genistein. The specification does not provide support that all the estrogen beta receptor agonist that has a higher relative potency for estrogen receptor beta compared to estrogen receptor alpha than that of genistein is useful in a method of reducing the incidence or severity of vascular hyperreactiivty in a patient. Also, it is known from the prior art that affinity selectivity does not necessarily ensure potency selectivity and the potency of the compounds does not always correlate directly with binding affinity (Meyers, J of Med Chem, 2001, 44, 24, p 4241, col 2, lines 3-6).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for estriol (examples 3 and 4) in a method of treating vasospasm and effect of estriol on diameter of coronary arteries does not reasonably provide enablement of reducing the incidence or severity of vascular hyperreactivity in a patient in need thereof comprising administering to the patient an effective amount of a selective estrogen beta receptor agonist that has a higher relative potency for estrogen receptor beta compared to estrogen receptor alpha than that of genistein. The

specification teach comparison of effects of estriol with 3βAdiol and epiestriol in vitro on Ca2+ responses in rhesus coronary VMC (example 9) and comparison of different estrogen beta receptor agonists (genistein, DPN). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention commensurate in scope with these claims. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the Invention:

The rejected claim is drawn to a method of reducing the incidence or severity of vascular hyperreactivity in a patient in need thereof comprising administering to the patient an effective amount of a selective estrogen beta receptor agonist that has a higher relative potency for estrogen receptor beta compared to estrogen receptor alpha than that of genistein.

(2) Breadth of the claims:

Claims 1- 16 are broad as they are drawn to a method of reducing the incidence or severity of vascular hyperreactivity in a patient in need thereof comprising administering to the patient an effective amount of a selective estrogen beta receptor agonist that has a higher relative potency for estrogen receptor beta compared to estrogen receptor alpha than that of genistein. The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims.

(3) Guidance of the Specification:

The guidance given by the specification to a method of reducing the incidence or severity of vascular hyperreactivity in a patient is 1) estriol in a method of treating vasospasm and effect of estriol on diameter of coronary arteries (examples 3 and 4) 2) comparison of effects of estriol with 3βAdiol and epiestriol in vitro on Ca2+ responses in rhesus coronary VMC (example 9) and comparison of different estrogen beta receptor agonists (genistein, DPN) 3) Measurement of estrogen receptor beta activity.

(4) Working Examples:

The specification provides example to a method of treating vasospasm by administration of the drug epiestriol and its effect on diameter of coronary arteries. The prior art teaches genistein and estradiol in a method of treating vasospasm and reducing the incidence or severity of vascular hyperreactivity in a patient.

5) The relative skill of those in the art:

The relative skill of those in the medical treatment art is high, requiring advanced education and training.

(6) The predictability of art:

Claims 1- 16 are broad as they are drawn to a method of reducing the incidence or severity of vascular hyperreactivity in a patient in need thereof comprising administering to the patient an effective amount of a selective estrogen beta receptor agonist that has a higher relative potency for estrogen receptor beta compared to estrogen receptor alpha than that of genistein. The claims are so broad and there is a high degree of unpredictability involved. Despite the advanced training in the medical treatment arts, the arts are highly unpredictable.

(7) The Quantity of Experimentation Necessary:

In order to practice the above claimed invention, one of ordinary skill in the art would have to first envision formulation, dosage, duration, route and, in the case of human treatment, an appropriate animal model system to test all the compounds for their selectivity towards estrogen receptors and then whether they are more potent towards beta receptor than alpha. Then the compounds need to be tested for their usefulness in a method of reducing the incidence or severity of vascular hyperreactivity in a patient in need thereof comprising administering to the patient an effective amount of the drug. If unsuccessful, one of ordinary skill in the art would have to envision a modification in the formulation, dosage, duration, route of administration etc. and appropriate animal model system, or envision an entirely new combination of the above and test the system again. The specification enables the treatment of vasospasm with estriol and shows comparison of estrogen receptor activities of few compounds namely, estriol, 3βAdiol, DPN, genistein and epiestriol. Claim 1 compasses a huge number of selective estrogen receptor beta agonists other than the compounds listed in the specification and

therefore, it would require undue, unpredictable experimentation to practice the claimed invention of comprising administering every single selective estrogen beta receptor agonist that has a higher relative potency for estrogen receptor beta receptor agonist than alpha than that of genistein. Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Umamaheswari Ramachandran whose telephone number is 571-272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER